Unveiling the Gut–Brain Axis: Potential Role of Probiotic Strains in Parkinson's Disease

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Abstract: *Parkinson's disease (PD) is a progressive neurological disorder associated with motor dysfunction, caused by degeneration of dopaminergic neurons in the substantia nigra, resulting in debilitating motor and non-motor symptoms. Moreover, the accumulation of α-synuclein in the enteric nervous system and loss of neurons highlights the disease involvement in the central nervous system. Gut dysbiosis is linked with the progression of Parkinson's disease (PD), which is further associated with the secretion of neurotoxic metabolites, intestinal permeability, and inflammation, resulting in increased neuronal damage. However, replenishing healthy gut microbiota through the administration of potential probiotic strains offers significant benefits in managing PD. Probiotics are defined as live microbial agents that show multiple therapeutic effects on various diseases, including neurological disorders. This review highlights the overview of emerging evidence related to the utilization of certain probiotic strains in the treatment of PD. Furthermore, research on clinical and pre-clinical effects of probiotic strains on pathophysiology is also studied, that suggests a promising result associated with motor symptom improvement and neuroprotection, which is considered a safe and novel treatment for enhancing the health of PD patients.*

KEYWORDS*: Dysfunction, Metabolites, Parkinson's disease, Probiotics, Gut, Neurological, Inflammation.*

1. Introduction

Parkinson's disease (PD) is considered to be the second most prevalent neurodegenerative disease worldwide (Vos *et al.,* 2016). The prevalence rate of Parkinson's disease has increased, with around 1.08 million new cases reported in 2019, resulting in the rise of 160%, as compared to figures from 1990 (Park *et al.,* 2023). It is marked by progressive degenerative disease of the central nervous system that shows a pathological impact on the basal ganglia (Ramesh and Arachchige, 2023; Krishnasamy, 2023). The condition of disruption in motor and non-motor neurological function of the human results in PD, these are mainly associated with dopamine deficiency, responsible for muscle tone and movement in substantia nigra pars compacta (SNc), as well as impairment in muscle rigidity, resting tremor and postural disability which is regarded as a hallmark of PD (Gazerani, 2019; Antony *et al.,* 2013; Stacy, 2011). The pathophysiological involvement of the gut-brain axis is demonstrated by the

non-motor symptoms, which include mood disorders, autonomic disturbances, gastrointestinal dysfunction, and cognitive decline that manifests before motor presentation. Growth factors, gut microbiota, oxidative stress and inflammatory pathways are some of the molecular and cellular processes that contribute to the pathophysiology of Parkinson's disease. The motor phenotype in PD is associated with changes in gut flora as suggested by some studies (Mirzaei *et al.,* 2022). The gastrointestinal system eventually becomes the most susceptible passage for pathogenic bacteria to enter in the human body. Therefore, these pathogenic bacteria are the prominent aetiology for such diseases.

Recent investigations have focused on alteration in the gut microbiome of PD patient. As gut microbiome consist of trillions of essential microbes that resides inside the gastrointestinal region and plays a pivotal role in the progression of PD (Cryan *et al.,* 2019; Kalyanaraman *et al.,* 2024). Typically, patient often exhibit lower abundance of short-chain fatty acid (SCFA) producing species such as *Roseburia intestinalis, Faecalibacterium prausnitzii* and other proinflammatory bacteria like *Escherichia/Shigella, Enterobacteriaceae* and *Akkermansia muciniphila* (Aho *et al.,* 2021; Cummings *et al.,* 1987). However, certain imbalance results in systematic inflammation, oxidative stress, disruption of intestinal barrier and elevated lipopolysaccharide (LPS) translocation factors affecting α-synuclein, causing aggregation in the enteric nervous system and brain (Park *et al.,* 2023). Probiotics are live microbial strains that improves health in multiple ways, when consumed in adequate amounts, it also has potential therapeutic approaches towards mitigating gut dysbiosis in Parkinson's disease patients. However, the most active species of probiotic strain are *Lactobacillus* or *Bifidobacterium* (Kerry *et al.,* 2018; Chandrasekaran *et al.,* 2024).

According to the preclinical studies, the probiotic species, namely, *Bacillus subtilis, Bifidobacterium longum* and *Lactobacillus plantarum* PS128 possess neuroprotective effects via numerous gut-brain axis pathways (Bongaerts *et al.,* 2016). For instance, *L. plantarum* PS128 enhances motor behaviour, upregulates neurotropic signaling, and controls inflammatory pathways of microRNA-155/SOCS1 in rotenone-induced PD animal models. Several studies on the gut-brain axis indicated the significant involvement of gut microbiota in controlling health and diseases through a complex interaction of neuronal, immunological, and metabolic signalling. However, these factors get changed in different conditions of PD, and its treatment is mainly focused on improving these sets of factors responsible for the disease (Catanzaro *et al.,* 2015; Tan *et al.,* 2021). The review highlights the recent findings that target the probiotic therapy which often shows adjunctive benefits in preventing neuroinflammation and progression of disease in PD patients. Research investigations have supported the hypothesis that targeted probiotic therapy may provide supplementary benefits in reducing neuroinflammation and slowing the progression of Parkinson's disease.

2. Microbiota-Gut-Brain Axis

Over the past decade, several studies have investigated the interactions between two complex systems, the gastrointestinal system and the brain, which further introduces to the gradual development of the concept of gut-brain axis. These findings were substantiated through the advanced experimental methodologies, physiological investigations and the researches employing functional magnetic resonance imaging (IMRI). Collectively, the data have shown a strong correlation between the central nervous system (CNS) and enteric nervous system (ENS). More recently, increasing interest towards the influence of gut microbiome has led to a broader perspective, which gives rise to the concept of the microbiota-gut-brain axis. Therefore, it underscores the bidirectional interconnection among the CNS, gastrointestinal system including the gut microbiota (Menozzi *et al.,* 2025).

2.1 Gut-Brain Neural Pathway in Parkinson's Disease

The bidirectional pathway between the CNS and GI tract involves various methods that has been utilized for investigating the axis including germ free models, studies related to infections, intervention studies and germ-free animal models (e.g., probiotics, prebiotics and antibiotics) (Bravo *et al.,* 2012). It is investigated that commensal microbial strains directly or indirectly impact the PD pathogenesis through circulatory and nervous systems. The neural connections for the GI tract are multi-tiered networking that starts with the mysenteric submucosal plexus and enteric glial cells. Notably, the gut lumen is

closely attached to the catecholaminergic neurons (Chesné *et al.,* 2019). According to de La Serre *et al.,* the mysenteric plexus is directly innervates by the vagus nerve, these neurons lead to the spinal cord's prevertebral ganglia and finally to higher brain regions. However, the terminals of vagal afferent neurons are located inside the gut mucosa which directly conveys information to the brain. It has been determined that these neurons are responsive towards lipopolysaccharides (LPS), which is an endotoxin secreted by gram-negative bacteria (de La Serre *et al.,* 2015). Elevated levels of LPS gradually activate vagal afferent neurons, which can lead to weight loss and hypophagia (reduced eating behaviour). Because these are common symptoms in PD, certain microbial communities that increase production of LPS and inflammatory cytokines may damage the intestinal epithelium and compromise gut barrier integrity in PD patients (van IJzendoorn *et al.,* 2019).

2.2 Bio functional activity of probiotics

Probiotics prominently demonstrate several mechanisms that have an effective impact on the gut microbiome, including antagonism, cross-feeding, and competition for nutrients, as well as binding sites on the intestinal lining (Wang *et al.,* 2021). Biofilms, which are three-dimensional bacterial colonies embedded in self-produced extracellular matrices that promote colonization and longer permanence in the host's mucosa, are one way that probiotic bacteria avoid pathogenic bacterial adhesion. Moreover, probiotics decrease luminal pH by producing organic acids such as lactic acid by *Lactobacillus* and *Bifidobacterium* species and also fight against pathogenic bacteria in the human gut and urinary tract (Reid *et al.,* 2011). The mechanism of gut microbiota in the pathogenesis of Parkinson's disease is demonstrated in the Fig 1. Hence, probiotics contribute to resistance toward other microorganisms, and it has been proven by a study that *Lactobacillus casei* has antagonistic properties against *Helicobacter pylori* while performing its eradication therapy.

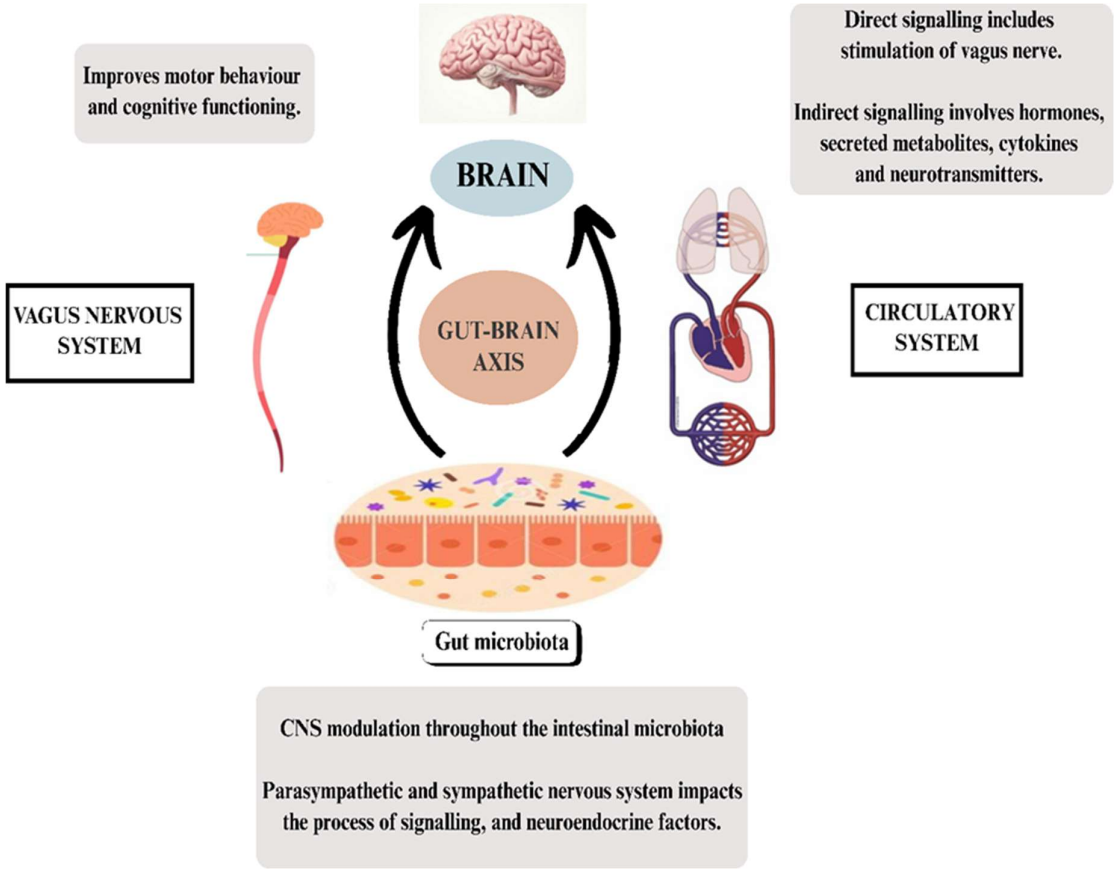

Fig. 1. The mechanism of gut microbiota in the pathogenesis of Parkinson's disease

The interaction between probiotics and native gut bacteria is another action known as cross-feeding that helps in increasing short-chain fatty acid production, such as butyrate, in the gut (Dalile *et al.,* 2019). Probiotics promote the activity of phagocytosis, production of individual immunoglobulins and down-regulating pro-inflammatory cytokines and up-regulating anti-inflammatory patterns. They contribute and maintain the integrity of the intestinal barrier by promoting mucin secretion and upregulating the expression of tight junction proteins, which prevents pathogenic microbes from adhering to overcome the intestinal barrier and shows the ability to produce neuroactive metabolites, such as serotonin, short chain amino acids (SCFA), g-aminobutyric acid (GABA), dopamine, and other neurotransmitter precursors, which may have positive impact on the gut-brain axis as these are illustrated in Table 1. Additionally, probiotics support in the breakdown of lactose through the actions of bile salt hydrolase and 8-galactosidase, which improves lactose malabsorption (Gangaraju *et al.,* 2022; Tan *et al.,* 2021).

Table 1. Role of secondary metabolites of probiotic strains on Parkinson's disease.

Metabolites	Activity	Relevance to PD	References
Short-Chain Fatty acids (SCFA)	Regulates the immune system, maintains gut inflammation	Butyrate promotes gut-brain axis communication and reduces neuroinflammation, Act as energy substrates for mitochondria and their fusion	(Dalile *et al.,* 2019; Unger *et al.,* 2016) (Donohoe *et al.,* 2011)
Organic acids	Lowers the intestinal pH	Maintains healthy gut microbiota	(Tamtaji *et al.,* 2019)
Exopolysaccharides	Antioxidant activity, modulates immunological functioning.	Decreases oxidative stress and enhances immune system in PD	(Fanning *et al.,* 2012; Wang *et al.,* 2021)
Neuroactive compounds	Is a serotonin, dopamine, & GABA producer;	Lessens anxiety and motor dysfunction in PD	(Dinan & Cryan, 2017; Tian *et al.,* 2022)

3. Probiotic-Induced Anti-Inflammation in Parkinson's Disease

Parkinson's disease (PD) is significantly associated with inflammation, from which the initial evidence arose in incidences related to encephalitis lethargica in cases that resulted from infection by influenza. Several viruses like influenza A, HSV-1, EBV, HIV, *Helicobacter pylori* and others have been linked to the development of PD (Iang *et al.,* 2009). Those neurotropic pathogens can gain access to the brain either through olfactory or enteric routes that activates the neuroinflammation of the nigrostriatal tract. Certain viral proteins also resemble that of alpha-synuclein (α-Syn) which then forms Lewy bodies (Maries *et al.,* 2003). Moreover, α-Syn also plays the role of a chemoattractant in the gut and it attracts immune cells leading to systemic and central inflammation in PD (Pajares *et al.,* 2020). In this context, probiotics may potentially reduce peripheral inflammation in PD preclinical and clinical trials, as demonstrated in a review study. Probiotic supplementation reduced the protein levels of inflammatory cytokines, such as IL-6 and TNF-α, in the brain and the periphery of PD models in preclinical studies. Notably, this anti-inflammatory effect was consistent regardless of the probiotic strain, type of PD model, or duration of the treatment. Although these results were partially confirmed in human research, where the peripheral region also showed decreased gene expression of related cytokines, including IL-1, IL-8, and TNF-α (Leta *et al.,* 2021). In the animal PD model and in small human individuals, probiotics have an impact that reduces oxidative stress, microglial activation, IL-6 and TNF-alpha, protects dopaminergic neurons, and improves motor and non-motor functioning (Panaitescu *et al*., 2024).

4. Clinical and Preclinical Evidence

Several studies provide evidence for the treatment of Parkinson's disease, in which different probiotic strains based on taxonomic classification, mostly with bacterial class Bacilli and actinobacteria with order *Lactobacillales* and *Bifidobacteriales,* such as *L. plantarum*, *L. acidophilus, L. reuteri, L. fermentum, etc*. These strains proved to show motor function, prevented dopaminergic neurons in vivo PD model, and enhanced gastrointestinal results, as elaborated in Table 2.

Table 2. Taxonomic classification of Probiotic strains associated with the treatment of PD

Bacterial Class	Order	Family	Genus	Species with evidences	References
Bacilli	*Lactobacillales*	*Lactobacillaceae*	*Lactobacillus*	*L. plantarum* various strains i.e., PS128, SG5, CCFM405, DP189) showed improved motor function, prevent dopaminergic neurons in vivo PD models in a 12-week pilot human case study.	Kim *et al.,* 2024; Lu *et al.,* 2021; Hong *et al.,* 2022; Dudek-Wicher *et al.,* 2020
Bacilli	*Lactobacillales*	*Lactobacillaceae*	*Lactobacillus*	*L. acidophilus, L. reuteri, L. fermentum* showed enhanced behavior, oxidative stress, and neuronal damage in animal PD models using a multi-strain mix.	Alipour Nosrani *et al.,* 2021; Atak *et al.,* 2024; Hong *et al.,* 2022
Bacilli	*Lactobacillales*	*Lactobacillaceae*	*Lactobacillus*	*L. casei, L. lactis* showed in human clinical mixtures; enhanced gastrointestinal results, non-motor symptoms.	Xiang *et al.,* 2022; Atak *et al.,* 2024; Hong *et al.,* 2022
Actinobacteria	*Bifidobacteriales*	*Bifidobacteriaceae*	*Bifidobacterium*	*B. bifidum, B. longum, B. infantis* showed improved gastrointestinal transit, inflammation, non-motor symptoms in human investigations.	Dudek-Wicher *et al.,* 2020 ; Xiang *et al.,* 2022; Atak *et al.,* 2024; Hong *et al.,* 2022
Actinobacteria	*Bifidobacteriales*	*Bifidobacteriaceae*	*Bifidobacterium*	*B. animalis subsp. lactis* (Bb12 or BS01) showed enhanced motor coordination in	Parra *et al.,* 2023; Magistrelli *et al.,* 2024;

				animal models, decreased motor and non-motor scores, and altered cytokines (IL-6, IFN-γ, and TGF-β) in clinical studies.	Martini *et al.,* 2022
Bacilli	Lactobacillales	*Enterococcaceae*	*Enterococcus*	*E. faecium, E. faecalis* as a multi-strain probiotics helped PD patients with their bowel movements and constipation.	Xiang *et al.,* 2022; Atak *et al.,* 2024
Bacilli	Lactobacillales	*Streptococcaceae*	*Streptococcus*	*S. thermophilus* showed that fermented milk formulations enhanced PD measures associated to constipation.	Xiang *et al.,* 2022; Atak *et al.,* 2024

A study by Tsao *et al.,* (2021) concluded that when *Lactobacillus salivarius* AP-32 was used as a probiotic bacterium in rats with 6-OHDA-induced lesions, results showed that an increased antioxidant activity leading to a reduction in oxidative stress and inflammation increase. There is a commensal that brings changes in fecal microbiota composition with a reduction in harmful bacteria. So, the motor impairment of PD caused by 6-OHDA-induced lesions was reduced due to the increased antioxidant activity of enzymes that combat dopaminergic cell death in the brain with either direct or indirect mode of action. Hence, *Lactobacillus salivarius* AP-32 was proven to be an effective probiotic that reduces the effect of Parkinson's disease by increasing antioxidant activity. Similarly, Yue *et al.,* (2022) indicated that when *L. lactis* MG1363-pMG36e-GLP-1 are used as a probiotic in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine MPTP-induced PD mice models, it resulted in a reduction in the ferroptotic signalling pathway. Additionally, *L. lactis* MG1363-pMG36e-GLP-1offers a potential pharmaceutical treatment for clinical prophylaxis, and managing PD by recovering intestinal microbial diversity, decreased iron deposition, reduced oxidative stress, and lipid peroxidation. Along with this, researchers have provided evidence that PD is mainly caused by oxidative damage which can be treated by supplementation of probiotics. When a mixture of probiotics containing *Lactobacillus acidophilus, Bifidobacterium bifidum, Lactobacillus reuteri,* and *Lactobacillus fermentum* supplemented in a group resulted in enhanced cognitive function, rotational behaviour, lipid peroxidation, and neuronal damage in comparison with other groups (Alipour Nosrani *et al.,* 2021; Park *et al.,* 2020).

According to Li *et al.,* (2022), *Bifidobacterium breve* CCFM1067 as probiotics in MPTP-Induced Mouse Models of PD showed prominent results that could be used as a supplement for preventing PD and its treatment through the gut-brain axis. The neuroprotective efficacy of Bifidobacterium breve Bif11strain in female rats administrated with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine hydrochloride (MPTP). This study also examined the molecular, behavioural and biochemical efficacy of B. breve Bif11 strains supplemented in MPTP-induced rat model having PD. The doses of probiotic strains administered in rats were about 1×10^{10} CFU and 2×10^{10} CFU for 21 days. Thus, the results have shown that *B. breve Bif11* has potential in improving symptoms like intestinal permeability, oxidative and nitrosative stress, tyrosine levels, short-chain fatty acid levels, motor and cognitive

functioning, and some inflammatory markers observed in PD patients (Ho *et al.,* 2018; Wang *et al.,* 2012; Skonieczna-Żydecka *et al.,* 2018).

The randomized controlled study by Ibrahim *et al.,* investigated the therapeutic effects of multi-strain probiotic formulation (Hexbio®) for the management of constipation in patients suffering from PD (Coffin *et al.,* 2011). During the intervention period of 8 weeks, Probiotic strains comprising of species *Lactobacillus* and *Bifidobacterium* with fructo-oligosaccharide are administered in PD patients, which further improved the efficiency of bowel opening frequency (BOF) and whole gut transit timing (GTT) as compared to placebo group. In addition to it, the probiotic group have showed higher reduction in GTT and greater mean in BOF which showed improved gastrointestinal motility. It was examined that probiotic-treated patients showed a five-fold increase in bowel frequency, indicating significant therapeutic benefits. On other side, no significant improvements were identified in motor and non-motor symptoms of PD. Therefore, this may reflect the specific target of gut associated outcomes (Ibrahim *et al.,* 2020).

Two double-blind, placebo-controlled randomized clinical trials (DBPC-RCTs) have generated class I evidences that has supported the effects of probiotic strains in the treatment of constipation in PD individuals. In one of the trials, around 120 patients suffering from PD were assigned a fermented milk product incorporated with multiple strains of probiotics namely, *L. delbrueckii* subsp, *Lactobacillus rhamnosus* GG, *L. acidophilus*, *L. plantarum*, *L. paracasei Bulgaricus, Streptococcus salivarius* subsp. *thermophilus*, *Enterococcus faecium, Bifidobacterium breve* and *B. animalis* subsp delivering a specific dose of 250×10^9 CFU, along with 125 g of prebiotic fiber for 4-week period. The result of this intervention which helped in showed a significant improvement in spontaneous bowel movement and stool consistency reducing reliance on laxatives (Barichella *et al.,* 2016).

Study by Atak *et al.,* (2024) investigated effect of probiotics strains on oxidative stress, motor symptoms and gastrointestinal dysfunction that is considered to be key concern in PD patients. Randomized controlled trials (RTCs) with placebo groups included 350 patients with Parkinson disease, supplemented with probiotics strains for over 4-12 weeks. Result showed increased improvement in PD ratings such gastrointestinal outcomes especially, enhancing the frequency of bowel movement and gut transit times, reduction in oxidative stress markers such as glutathione and malondialdehyde. Overall, it serves as a supportive treatment for PD patients by treating gut-brain dysfunction. Hsieh *et al.,* (2020) demonstrated that administrating probiotics supplements to Mito Park mice significantly, improves motor performance and reduced the loss of dopaminergic neurons. After receiving probiotic supplements for 12 weeks, the improvement in gastrointestinal symptoms, as well as drop in IL-6 and IFN-sh with increase in concentration of TGF-B was noticed (Magistrelli *et al.,* 2024). Moreover, the administration of Vitamin D with probiotic strains have resulted into a significant drop in IL-1b, IL-6, INF-g, and MDA values, which has also raised TAC and IL-10 levels, declining the intensity of anxiety levels, according to the study (Zali *et al.,* 2024; Borzabadi *et al.,* 2018).

Furthermore, Hashish and Salama (2023) emphasized the association between the brain and the gastrointestinal system, including the possibility of microbiome-based therapy, and the intestinal dysbiosis associated with Parkinson's disease (PD), which is characterized by disrupted metabolic pathways and a decrease in anti-inflammatory bacteria. In the encephalopathy ring agreement (MPTP) mouse model, Wang *et al.,* (2023) examined that ingesting *Clostridium butyricum,* which secretes GLP-1 that reduces PD symptoms by balancing microbial strains, enhancing mitophagy, and reducing oxidative pressure via the GLP-1R pathway. Likewise, *Lactobacillus plantarum* DP189 preserves the dopaminergic neurones in the PD models, reduces 3-synuclein polymers, and enhances the colony of gut bacteria (Wang *et al.,* 2022). Other than this, Kim *et al.,* (2024) state that the probiotic formulation SLAB51 has a neuroprotective effect through reducing inflammation, stimulating cognitive function, and modulating the intestinal microbiota. Moreover, it has also been revealed that a synbiotic combination enhances the levels of dopamine and motor co-ordination in PD rats by addressing microbial imbalance and increasing the amount of short-chain fatty acids (Mehrabani *et al.,* 2023) as demonstrated in Table 3.

Table 3. Summary of recent evidences examining the probiotic effects in animal models of Parkinson disease

Sr. No	Study Model	Probiotics	Frequency of Use	Metabolic effects	References
1.	Rodent Mice	*Lacticaseibacillus rhamnosus* HA-114	6 weeks	No effect on anxiety, Improved hippocampal-dependent cognition deficits.	Xie *et al.,* 2020
2.	MPTP-induced PD mouse model	*Bifidobacterium breve* CCFM1067	5 weeks	↑ Short-chain fatty acids → linked to anti-inflammatory action.	Li *et al.,* 2022
3.	Mice with hippocampal memory extinction	*Bifidobacterium breve* A1 (MCC1274)	4 consecutive days	Restores hippocampal synaptic plasticity, regulates neuropsin expression results in improvement of cognitive functioning.	Ishii *et al.,* 2021
4.	MPTP-induced PD mouse model	*Bifidobacterium animalis subsp. lactis* NJ241 (NJ241)	-	↑ Short-chain fatty acids, enhances intestinal GLP hormone, activates nigral PGC-1α (Peroxisome Proliferator-Activated Receptor Gamma Coactivator-1 Alpha) signalling.	Dong *et al.,* 2024
5.	Male rats	*Lactobacillus paracasei*	28 days	Results in neuroprotective and motor-improving effect	Khandestan (2020)
6.	Male albino Wistar rats	*Streptococcus thermophilus, Bifidobacterium lactis, Bifidobacterium lactis. Lactobacillus acidophidophilus Lactobacillus helveticus Lactobacillus paracasei Lactobacillus plantarum Lactobacillus brevis*	Oral administration (4 weeks)	Reduces neuroinflammation, enhances gastric emptying, protects neurons, and improves motor deficits.	Sharma *et al.,* 2025
7.	Early-stage PD male albino rat model	Multi-strain probiotic strains suspension	-	Improves gut integrity, Prevents the reduction of SCFA metabolites, reduced tyrosine hydroxylase (TH)-positive cell loss by 17% in comparison to a placebo, Lowers the neurodegeneration and neuroinflammation.	Sancandi *et al.,* 2023
8.	PD male mice model	*Lactobacillus plantarum DP189*	Oral administration	Improves capacity for behaviour.	Wang *et al.,* 2021

			(14 days)	Elevated levels of 5-hydroxytryptamine and dopamine. Tyrosine hydroxylase (TH) cells have a higher positive rate. AKT/mTOR and ERK2 pathways were activated.	
9.	PD mouse model	*Bifidobacterium breve BBr60*	-	Increased SCFA, NLRP3/NLRP6 inflammasome balance was restored, Reduces gut dysbiosis.	An *et al.,* 2025
10.	PD rat model	*Lactobacillus rhamnosus* (10^8–10^9 CFU, oral) + Curcumin	Oral doses (21 days)	Improvement in behavioural parameters also acetylcholinesterase (AChE) activity. - lowers oxidative stress markers, Shows neuroprotective improvement by synergistic effects of curcumin with probiotics species.	Soni *et al.,* 2025

Incorporation of probiotics, prebiotics and faecal microbiota transplantation (FMT) is very critical in order to enhance microbial colonies. Nevertheless, one should be aware of such barriers as the need to demonstrate a remarkable method of management, standardization of clinical operations, and optimization of strains (Benvenuti *et al.,* 2024). Specifically, *Lacticaseibacillus rhamnosus* E9 exerted neuroprotective effects in MPTP-induced PD mice, and it could alter gut microbiota, maintain intestinal barrier integrity, and also attenuate oxidative stress and thus it could be a beneficial supplement (Aktas *et al.,* 2024). Other different findings are also summarized in Table 4.

Table 4. Studies associated with the efficacy of probiotic strains on PD in human model.

SR.No	Study design	Probiotic strains	Duration	Sample size	Mechanism outcomes	References
1.	Double-blind RCT	Multi-strain (*L. acidophilus*, *B. bifidum*, *L. fermentum*, *L. reuteri*)	12 weeks	60 PD patients	Decreased inflammation and improved oxidative status	Tamtaji *et al.*, 2019
2.	Non-randomized pilot study	Varied strains in probiotic yogurt	4 weeks	40 PD patients	Mild motor benefits, neuroinflammation modulation.	Cassani *et al.,* 2011
3.	Systematic Review	–	–	7 RCTs analyzed	Regulates gut-brain axis, inflammatory actions	Sun & Shen (2020)
4.	RCT	*E. faecium, Streptococcus thermophilus*,	8 weeks	50 PD patients	altered cytokine status, modify intestinal barrier	Ibrahim *et al.,* 2020

5.	Open-label trial	*B. animalis, Lactobacillus rhamnosus GG*	8 weeks	30 PD patients	Elevated SCFA production, balance the gut microflora	Georgescu *et al.,* 2016
6.	Randomized control trial	*Actinobacteria, Negativicutes, Bacillus.*	12 weeks	50 PD patients	Improvements in Rapid Eye Movement Sleep Behaviour Disorder (RBD) symptoms and motor function,	Du *et al.,* 2025
7.	Clinical trials	*Lactobacillus rhamnosus NCDC17*	-	42 PD patients with rat model	Lower the *Lactobacillus* and Bacteroides which predicts progression of PD, Regulates miR-146a and GDNF expression.	Wei *et al.,* 2021

5. Future Perspective of Probiotics Strains in Parkinson's Disorder

New technologies are highlighting real-time studies in humans, which allows researchers to track how microbial strains integrate into the gut microbiota (Xie *et al.,* 2023; Hong *et al.,* 2022). In future, routine health checkups includes detail reports on different types of probiotic strains present in the body, and how these factors influence human body. Innovative sampling techniques provide clear insights into how probiotics affect the mechanism in body especially, metabolism, immunity and overall microbiome. This will lead to broaden the approach towards medicine. Researchers can even better understand the optimal dosage according to the needs of patient health. Moreover, understanding specific active compounds will help in the developments of postbiotics (Spacova *et al.,* 2023).

Emerging evidences may contribute to the future goals where essential microbes are utilised to tackle major global challenges especially lowering the risks of various diseases as well as negative impact of pandemics (Zmora *et al.,* 2019). There is important need to conduct further studies to establish the sustainability of using probiotics to restore the protein and oxidative balance in the enteric nerve system (ENS) of PD patients (Zhu *et al.,* 2022). There is also uncertainty on whether probiotic use results in intestinal colonisation that is permanent or whether the microbiota returns to its pre-treatment state. However, treatment outcomes could be enhanced by personalized probiotic therapy, where probiotics are selected based on the profile of a given patient's gut microbiota. The demand for strain-specific activity and product quality should be met, as the manufacturing processes will influence cell safety and probiotic activity. Lastly, it is necessary to conduct additional clinical trials that could prove their therapeutic value in the treatment of PD (Castelli *et al*., 2021).

6. Conclusion

Parkinson’s disease (PD) is considered to be a neurodegenerative disorder that involves both motor and non-motor symptoms, which is affected by the disruption in the gut-brain axis. However, probiotic therapy emerges as a promising adjunctive approach in the management of PD by reducing inflammation, restoring the microbiome, regulating intestinal barrier function and immunomodulatory metabolites. According to the clinical and preclinical surveys, it has been concluded that various probiotic strains with beneficial therapeutic effects, such as *Lactobacillus salivarius, Lactobacillus plantarum*, *Bifidobacterium breve, L. lactis, Lactobacillus acidophilus, Bifidobacterium bifidum, Lactobacillus reuteri,* and *Lactobacillus fermentum, L. delbrueckii* subsp., *Lactobacillus rhamnosus* GG, *L. acidophilus*, *L. plantarum*, *L. paracasei Bulgaricus, Streptococcus salivarius* subsp.

thermophilus, *Enterococcus faecium, Bifidobacterium breve* and *B. animalis* subsp, *Lacticaseibacillus rhamnosus, Clostridium butyricum,* as well as a combination of *Lactobacillus* and *Bifidobacterium* with fructo-oligosaccharide and certain synbiotic formula improves dopamine levels, cognitive and motor functioning, modulating inflammatory pathways and also enhances the antioxidant activity. Vitamin D supplemented with probiotics strains has shown potential in alleviating anxiety symptoms. Thus, probiotics can be an effective treatment method for Parkinson's disease, particularly patient with neurological and gastrointestinal disorders.

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None declared

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Declaration of Competing Interest
I declare that the manuscript, or part of it, has neither been published (except in form of abstract or thesis) nor is currently under consideration for publication by any other journal; and that my co-authors have read the manuscript and approved its submission to Journal of Food and Humanity. On behalf of all authors, I also confirm that we do not have any actual or potential conflict of interest.

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Conflict Of Interest
The authors declare that there is no conflict of interest.
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